Three Faces of Fragile X Syndrome

Cornelia Lieb-Lundell
*University of St. Augustine for Health Sciences, clieb@usa.edu*

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THREE FACES OF FRAGILE X SYNDROME

Fragile X (FXS) - Fragile X primary ovarian insufficiency (FXPOI) - Fragile X tremor/ataxia syndrome (FXTAS)

Cornelia Lieb-Lundell PT, DPT, MA, PCS
University of St. Augustine for Health Sciences, San Marcos, CA

Fragile X is associated with a change to the FMR1 gene of the chromosome Xq27.3. This single FMR1 gene change will result in Fragile X-associated Disorders which includes three disorders that can cover multi generations in one family. PT interventions must vary accordingly.

**FRAGILE X**

- >200 CGG Repeats in the FMR1 gene
- Full FXS transmitted by mother to $\varnothing$ or $\varnothing$ (milder)
- All offspring from a FXS males will be typical

**Activity Limitations**
- Decreased motor and intellectual development
- Inability to communicate age appropriately
- Limited social contact with limited peer interaction

**Body structure Impairments**
- Soft skin
- Pectus excavatum
- Mitral valve collapse

**FRX PRIMARY OVARIAN INSUFFICIENCY**

- 55–200 CGG Repeats in the FMR1 gene (premutation range)
- Transmitted from female carrier to 50% of female offspring who are then carriers

**Impairments in Childhood and Adolescence**
- Social anxiety to point of depression or extreme shyness and/or social ineptness
- ADHD

**Body structure Impairments as an Adult**
- Premature menopause (±5 years earlier than non-carrier) related to Primary ovarian insufficiency
- Early onset osteopenia progressing to osteoporosis
- Coronary heart disease
- Thyroid dysfunction
- Fibromyalgia and/or undifferentiated muscle pain
- Anxiety disorder
- Monitor at ±50 years for symptoms of FXTAS

**Activity Limitations**
- Limited endurance, consider FXPOI as a basis

**FXTAS FRX TREMOR/ATAXIA SYNDROME**

- 55-200 CGG Repeats in the FMR1 gene (premutation range)
- Transmitted from male parent to all daughters but not to sons, daughters will be carriers

**Body structure Impairments**
- >50 years on-set of action/intention tremor and cerebellar ataxia or parkinsonism
- Cerebellar atrophy and increased T2 signal intensity in the middle cerebellar peduncles
- Balance problems with ataxia
- Cognitive decline, poor judgment and mood instability
- Numbness of the extremities, neuropathy

**Activity Limitations**
- Gait instability with increasing falls
- Decreasing ability to carry out ADL skills
- Difficulty executing job responsibilities
- Decreased sexual function
- Driver safety risk with declining safety awareness

**PHYSICAL THERAPY IMPLICATIONS** ~The Therapist’s primary task: to participate in the differential diagnosis process. The Therapist’s secondary task: to obtain a complete family history which should include the question: is there a family history of intellectual disabilities or autism spectrum disorders. This leads to the following interventions:

- Support developmental progress and postural control
- Biomechanical management for joint instability
- Develop, implement and monitor ongoing exercise program
- Develop ability to participate in peer activities
- Treat presenting impairment(s)
- Teach osteoporosis prevention and management
- Support implementing a regular exercise routine
- Differentiate normal aging from development of FXTAS
- Differentiate from other movement disorders i.e. parkinsonism
- PT identify and address cerebellar dysfunction, classify the ataxia
- Functional training to address limitations
- PT support to identify and implement adaptations

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